C6

54. (amended) The molecular library of retroviruses according to claim 47, wherein said candidate bioactive peptide is fused to a nucleic acid sequence encoding a targeting sequence.

55. (amended) The molecular library of retroviruses according to claim 47, wherein said candidate bioactive peptide is fused to a nucleic acid sequence encoding a rescue sequence.

56. (amended) The molecular library of retroviruses according to claim 47, wherein said candidate bioactive peptide is fused to a nucleic acid sequence encoding a stability sequence.

57. (amended) The molecular library of retroviruses according to claim 47, wherein said candidate bioactive peptide is fused to a nucleic acid sequence encoding a dimerization sequence.

REMARKS

Claims 23-26, 28-30, 32, 34-37, 40-52 and 54-57 are pending after entry of the amendments set forth herein.

Claims 23-58 were examined and were rejected. No claims were allowed. Claims 23-26, 28, 29, 30, 34, 35, 36, 37, 40-44, 47-52 and 54-57 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. No new matter is added by these amendments. Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Support for the amending language "candidate bioactive peptide" may be found in the specification on page 5, lines 5-14. Support for the amending language "peptide of from 4 to 100 amino acids in length" may be found on page 5, lines 15-22. Support for the amending language "randomized portion" may be found in the specification on page 6, line 2. Support for the amending language of "the sequence set forth in SEQ ID NO:47" may be found in the specification on page 22, line 27.

A substitute CRF is attached herewith.

Claims 47-58 have been rejected under 35 U.S.C. 101 as directed to non-statutory subject matter. The Office Action states that library would read on naturally occurring retroviruses or cells comprising such retroviruses, which undergo mutations similar to the instantly claimed biased random library. Applicants respectfully submit that the presently claimed library does not read on naturally occurring retroviruses or cells. The claims specifically recite a library comprising a large number of different retroviral sequences comprising an insertion encoding 4 to 100 amino acids with a randomized

portion biased to minimize stop codons. Such a library could not occur in nature, and does not read on a natural product.

The Office Action further states that libraries are starting materials, and not a useful product. Applicants respectfully submit that the library set forth in Claims 47-58 meets the requirements of 35 U.S.C. 101 for utility. An invention has a well-established utility if a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention *(e.g.,* properties or applications of a product or process), and the utility is specific, substantial, and credible. Applicants respectfully submit that the use and sale of libraries of compounds is well known in the biological and chemical arts. The development of libraries having novel features is important in the field of molecular biology. For example, attached herewith is an offer for sale of a retroviral cDNA expression library. One of skill in the art would appreciate the commercial value of such libraries, and their utility in the molecular biology workplace. The Patent Office has recognized the utility and commercial value of libraries of agents, and may such libraries have been patented.

A claimed invention must have a specific and substantial utility. This requirement excludes "throw-away," "insubstantial," or "nonspecific" utilities, such as the use of a complex invention as landfill, as a way of satisfying the utility requirement of 35 U.S.C. 101. The presently claimed invention meets such requirements, because the claimed library provides a means of screening for randomized bioactive agents, and is specifically useful in the methods of the invention.

A rejection based on lack of utility should not be maintained if an asserted utility for the claimed invention would be considered specific, substantial, and credible by a person of ordinary skill in the art in view of all evidence of record. Office personnel are reminded that they must treat as true a statement of fact made by an applicant in relation to an asserted utility, unless countervailing evidence can be provided that shows that one of ordinary skill in the art would have a legitimate basis to doubt the credibility of such a statement.

In view of the above amendments and remarks, withdrawal of the rejection under 35 U.S. 101 is respectfully requested.

Claims 23-58 have been rejected under 35 U.S.C. 112, first paragraph as enabled only for the specific libraries provided in Figs. 1 and 2. Applicants respectfully submit that the presently claimed invention meets the requirements of 35 U.S.C. 112, first paragraph.

The present claims recite a retroviral sequence comprising an insertion of a randomized peptide coding sequence, which sequences are expressed in said cells to produce a plurality of randomized peptides. One of skill in the art could readily utilize the teachings of the present application to practice

the claimed methods, and produce the claimed compositions. The specification provides ample guidelines for the utilization of vectors.

The randomization of sequences, and the use of a bias to minimize stop codons, is described in detail on page 20, line 29, to page 21, line 19. Methods to bias the peptide for interaction with a known class of molecules is described in detail on page 20, line 20, to page 23, line 12. Retroviral constructs useful in the invention are described in detail on page 24, line 22 to page 29, line 24. The specification includes guidelines for the practitioner in the area of promoter selection, virus construction, randomization of the peptide coding sequence and introduction of the retroviral sequence into a cell. One of skill in the art could readily practice the claimed invention.

The determination of enablement is performed in view of the methods that are reasonably predicted from the provided experimental data, from the field of use for the claimed methods, and from the level of skill in the art. The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). See also *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988)

"Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." *In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).* One may assess these factual consideration by juxtaposing the breadth of the independent claim, and the examples and guidance proffered by Applicants, and review them in view of the knowledge in the art. *Ajinomoto Co. Inc. v. Archer-Daniels-Midland Co., 1996 U.S. Dist. LEXIS 15989.*

Practice of the claimed invention would not require undue experimentation by one of skill in the art. In order to practice the invention, one of skill in the art needs to know the parameters for several aspects of the claimed method. Coding sequence and vector selection and transfection of the vector into appropriate cells are required to practice the invention. Guidance for the practice of these steps is disclosed in the subject application.

It is well known in the art that protein expression is dependent on the host cell, expression vector, regulatory elements, etc. In fact, the literature provides ample guidance for selecting the appropriate combination of elements, vectors and cells. See, *e.g.*, Nolan *et al. Curr Opin Biotechnol* 1998 **9**:447-450, Verma *et al. J Immunol Methods* 1998, **216**:165-181 and Sambrook *et al. Molecular Cloning: A Laboratory Manual*, CSH Press 1989. A variety of methods are commonly used to construct

vectors for expression in bacteria, mammalian cells, insect cells, retroviruses and *in vitro*, and a variety of suitable promoter and enhancer sequences are known in the art. In view of the methods known in the art, and disclosure of the exemplary constructs, the specification is fully sufficient to describe the claimed constructs in clear and concise terms, and shows possession of the same.

Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. Appellants note that recitation in a claim of a generic element, (for example promoters, retrovirus, *etc.*), does not require that the specification list each and every promoter that might be used with the invention. Rather, one may rely on the thousand of promoters known in the art to be useful in initiation transcription of a proximal gene. Indeed, as set forth in the MPEP: a patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies , Inc* ., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

In conclusion, Appellants respectfully submit that the present claims meet the requirements of 35 U.S.C. 112, first paragraph. The law does not require that every detail of the working examples be reiterated as a limitation in the claims. It is not required that the applicant provide a working exemplification for every embodiment of a claim, nor to spell out every detail. See MPEP 608.01(h) "A patent specification is not intended nor required to be a production specification". Withdrawal of the rejection is requested.

Claims 25-58 have been rejected under 35 U.S.C. 112, second paragraph as vague and indefinite. The Office Action states that the claims fail to point out what is excluded or included by the claim language. Applicants respectfully submit that the present claims meet the requirements of 35 U.S.C. 112, second paragraph.

Claims 23 and 24 have been stated to be unclear as to whether an altered cell phenotype or bioactive agent is being screened. The claims have been amended to specifically recite that the screening method identifies a cell with an altered phenotype resulting from expression of a bioactive peptide. Withdrawal of the rejection is requested.

The Examiner has objected to the use of the term "minimize" in the claims. Applicants respectfully submit that the use of relative terms, such as minimize, is allowable in patent claims. Under the law pertaining to indefiniteness, if the claims, read in light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is

as precise as the subject matter permits, the courts can demand no more. See *Hybritech v. Monoclonal Antibodies* 231 U.S.P.Q. (BNA) 81, *Shatterproof Glass Corp. v. Libbey-Owens Ford Co.*, 758 F.2d 613, 624, 225 U.S.P.Q. (BNA) 634, 641 (Fed. Cir. 1985). The present application provides clear guidelines for means of minimizing stop codons in the randomized portion of a candidate bioactive peptide (see specification on page 20, line 29 to page 21, line 10). To alleviate the problem of stop codons interfering with peptide synthesis, random residues are encoded as NNK, where K=T or G. This allows for encoding of all potential amino acids (changing their relative representation slightly), but importantly preventing the encoding of two stop residues TAA and TGA. Thus, libraries encoding a 10 amino acid peptide will have a 15.6% chance to terminate prematurely.

The Office Action states that the metes and bounds of the terms "phenotype", "cell", "transdominant intracellular bioactive agent", "molecular library of biased randomized nucleic acids", and "classes of molecules", are unclear. Applicants respectfully submit that the meaning of these terms is clear to one of skill in the art, in view of the teachings of the specification.

The present application states that suitable phenotypic changes include, but are not limited to: gross physical changes such as changes in cell morphology, cell growth, cell viability, adhesion to substrates or other cells, and cellular density; changes in the expression of one or more RNAs, proteins, lipids, hormones, cytokines, or other molecules; changes in the equilibrium state (i.e. half-life) or one or more RNAs, proteins, lipids, hormones, cytokines, or other molecules; changes in the localization of one or more RNAs, proteins, lipids, hormones, cytokines, or other molecules; changes in the bioactivity or specific activity of one or more RNAs, proteins, lipids, hormones, cytokines, receptors, or other molecules; changes in the secretion of ions, cytokines, hormones, growth factors, or other molecules; alterations in cellular membrane potentials, polarization, integrity or transport; changes in infectivity, susceptibility, latency, adhesion, and uptake of viruses and bacterial pathogens; etc. By "capable of altering the phenotype" herein is meant that the bioactive agent can change the phenotype of the cell in some detectable and/or measurable way (see specification, page 31, lines 21-31). The meaning of the term "cell" is well understood in the art.

Transdominant intracellular bioactive peptide refers to the peptide encoded by the construct, as set forth in the claims. "Transdominant" herein is meant that the bioactive agent indirectly causes the altered phenotype by acting on a second molecule, which leads to an altered phenotype. A transdominant effect is a distinguishable effect by a molecular entity (i.e., the encoded peptide or RNA) upon some separate and distinguishable target; that is, not an effect upon the encoded entity itself. As such, transdominant effects include many well-known effects by pharmacologic agents upon target

molecules or pathways in cells or physiologic systems. A transdominant effect upon a protein or molecular pathway is clearly distinguishable from randomization, change, or mutation of a sequence within a protein or molecule of known or unknown function to enhance or diminish a biochemical ability that protein or molecule already manifests (see specification, page 32, line 23 to page 33, line 25).

The nature of the molecular library of biased randomized nucleic acids has been clarified in the language of the claim. As described above, the specification provides ample support for methods of randomizing and biasing peptide coding sequences. Withdrawal of the rejections is requested.

The office Action states that Claim 24 is confusing as to whether the phenotype alteration is due to interaction of biased residues to a class of molecules. Applicants respectfully submit that it is not necessary for the claim to specifically recite the nature of the interaction between the bioactive peptide and the cell. Due to the bias in the library, it is expected that there will be a bias in the nature of interactions, however, such is not required for the successful practice of the method.

Claims 25 and 26 have been rejected as not further limiting the base claim from which they depend. Applicants respectfully submit that the identification of a bioactive peptide, as set forth in Claims 23 and 24, need not comprise an isolation step. Many schemes are known in the art, in which one can identify a sequence through positioning, not through isolation. Therefore, the steps recited in Claims 25 and 26 are not inherently a part of the base claim, and do provide a limitation of the base claim. Withdrawal of the rejection is requested.

Claim 29 is stated to be confusing as to molecules included in the SH3 or SH2 domains or death domains, and to other recited compounds. Without conceding to the correctness of the rejection, in order to further prosecution, Claim 29 has been amended to recite a specific SH3 targeting sequence of interest. Withdrawal of the rejection is requested.

The Office Action states that Claims 30, 38-46, and 53-56 broadens the base claim, which does not recite a presentation sequence. Applicants respectfully submit that the dependent claims do limit the base claim. The group of molecules comprising sequences both with and without a fusion partner is clearly generic to the subgroup comprising sequences with a fusion partner. Withdrawal of the rejection is requested.

The Office Action states that claims 33-37 are unclear as to whether exponential numbers refer to different amino acids in the library, or the size of the library. The claims have been clarified, and

recite that the exponential numbers refer to the size of the library. Applicants respectfully submit that the term "at least" is commonly used in patent claims to refer to a minimum, and is clear to one of skill in the art. Applicants are not required to state a maximum size for a corresponding upper limit. Withdrawal of the rejection is requested.

Claims 23-46 have been rejected under 35 U.S.C. 101 for statutory double patenting over claims 1-27 of U.S. Patent no. 6,153,380. Claim 23-46 have been rejected under the judicially created doctrine of obviousness type double patenting over claims 1-12 of U.S. Patent no. 6,365,344. Claims 23-46 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 23-38 of copending Application 09/727,715; 09/916,940; 08/963,368; or 08/787,738, now issued as U.S. Patent no. 6,455,247.

In determining whether a statutory basis for a double patenting rejection exists, the question to be asked is: Is the same invention being claimed twice? 35 U.S.C. 101 prevents two patents from issuing on the same invention. "Same invention" means identical subject matter. *Miller v. Eagle Mfg.* Co., 151 U.S. 186 (1984); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Ockert,* 245 F.2d 467, 114 USPQ 330 (CCPA 1957). The pending claims and the claims of the '380 patent are not identical. The present claims specifically recite a randomized sequence biased to minimize stop codons; and a randomized sequence biased to interact with a class of molecules. Such elements are not present in the claims of the '380 patent and therefore are not statutory double patenting.

Further, the claimed invention is not obvious in view of the claims of the '380, the '344 patent, or in the copending applications cited above. In determining whether a nonstatutory basis exists for a double patenting rejection, the first question to be asked is - does any claim in the application define an invention that is merely an obvious variation of an invention claimed in the patent? Obviousness-type double patenting requires rejection of an application claim when the claimed subject matter is not patentably distinct from the subject matter claimed in a commonly owned patent when the issuance of a second patent would provide unjustified extension of the term of the right to exclude granted by a patent. See *Eli Lilly & Co. v. Barr Labs.*, Inc., 251 F.3d 955, 58 USPQ2d 1865 (Fed. Cir. 2001); *Ex parte Davis*, 56 USPQ2d 1434, 1435-36 (Bd. Pat. App. & Inter. 2000).

A double patenting rejection of the obviousness-type is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. *In re Braithwaite*, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, any analysis employed in an obviousness-type double patenting rejection parallels

the guidelines for analysis of a 35 U.S.C. 103 obviousness determination. *In re Braat*, 937 F.2d 589, 19 USPQ2d 1289 (Fed. Cir. 1991); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Since the analysis employed in an obviousness-type double patenting determination parallels the guidelines for a 35 U.S.C. 103(a) rejection, the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 are employed when making an obvious-type double patenting analysis. When considering whether the invention defined in a claim of an application is an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art.

One of skill in the art, upon reading the claims of the above-cited applications and patents, would not reasonable expect to be able to produce or use a library comprising a randomized sequence biased to minimize stop codons; and a randomized sequence biased to interact with a class of molecules. Such features are not an obvious variation of the cited claims. There is no suggestion of such a library. Whether such a library would be dominated by the generic claims of the '380 patent or the '344 patent is not relevant.

As stated in the MPEP, section 804 "domination and double patenting should not be confused". They are two separate issues. One patent or application "dominates" a second patent or application when the first patent or application has a broad or generic claim, which fully encompasses or reads on an invention defined in a narrower or more specific claim in another patent or application. **Domination by itself cannot support a double patenting rejection**. *In re Kaplan*, 789 F.2d 1574, 1577-78, 229 USPQ 678, 681 (Fed. Cir. 1986); and *In re Sarrett*, 327 F.2d 1005, 1014-15, 140 USPQ 474, 482 (CCPA 1964).

Applicants respectfully submit that the present claims are directed to an unobvious invention, and are not the same invention, or made obvious by, claims 1-27 of U.S. Patent no. 6,153,380; claims 1-12 of U.S. Patent no. 6,365,344, or claims 23-38 of copending Application 09/727,715; 09/916,940; 08/963,368; or 08/787,738, now issued as U.S. Patent no. 6,455,247. Withdrawal of the rejection is requested.

In view of the above remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issue.

If the Examiner finds that a Telephone Conference would expedite prosecution of this application, he is invited to contact the undersigned (650) 327-3400.

In the event that the transmittal letter is separated from this document and the Patent Office determines that extensions or other relief is required and/or fees are due applicants, the Applicant petitions for any required relief, including extensions of time, and authorize the Commissioner to charge our Deposit Account No. 50-0815, Order Number RIGL-004CON3, for any fees due in connection with the filing of this document. The Patent Office is not authorized to charge issue fees to our Deposit Account.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: December 16, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

23. (amended) A method for *in vitro* screening for [a transdominant intracellular bioactive agent capable of altering the phenotype of] a cell whose phenotype is altered by expression of a transdominant intracellular bioactive peptide, said method comprising the steps:

a) introducing a molecular library comprising at least 10^4 different retroviral nucleic acid sequences, [of biased randomized candidate nucleic acids] into a plurality of cells, [wherein each of said nucleic acids comprises a different nucleotide sequence] wherein said retroviral nucleic acid sequences comprise an insertion of a nucleic acid sequence encoding a candidate bioactive peptide of from 4 to 100 amino acids in length, wherein said candidate bioactive peptide comprises a randomized portion[, wherein said biased randomized candidate nucleic acids are] biased to minimize stop codons, and wherein said [randomized candidate nucleic acids] retroviral nucleic acid sequences are expressed in said cells to produce a plurality of randomized peptides;

b) screening said plurality of cells [for] to detect a cell exhibiting an altered phenotype[, wherein said altered phenotype is] due to the [presence] expression of a transdominant bioactive [agent] peptide[; and

c) identifying said transdominant bioactive agent].

24. (amended) A method for in vitro screening for [a transdominant intracellular bioactive agent capable of altering the phenotype of] a cell whose phenotype is altered by expression of a transdominant intracellular bioactive peptide, said method comprising the steps:

a) introducing a molecular library comprising at least 10^4 different retroviral nucleic acid sequences, [of biased randomized candidate nucleic acids] into a plurality of cells, [wherein each of said nucleic acids comprises a different nucleotide sequence] wherein said retroviral nucleic acid sequences comprise an insertion of a nucleic acid sequence encoding a candidate bioactive peptide of from 4 to 100 amino acids in length, wherein said candidate bioactive peptide comprises a randomized portion[, wherein said biased randomized candidate nucleic acids are] biased to interact with a class of molecules and wherein said [randomized candidate nucleic acids] retroviral nucleic acid sequences are expressed in said cells to produce a plurality of randomized peptides;

b) screening said plurality of cells [for] to detect a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the [presence] expression of a transdominant bioactive [agent] peptide[; and

c) identifying said transdominant bioactive agent].

25. (amended) A method according to claim 23 or 24 further comprising the step:

[d)] isolating said cell exhibiting an altered phenotype.

26. (amended) A method according to claim 25 further comprising the step:

[e) isolating said candidate nucleic acid from said cell] identifying said nucleic acid encoding said candidate bioactive peptide or identifying said candidate bioactive peptide.

28. (amended) [A] The method according to claim 23 wherein said [biased randomized candidate nucleic acids comprise] randomized portion comprises codons [comprising] having the sequence NNK, wherein N is selected from the group consisting of A, T, C and G, and K is selected from the group consisting of T and G.

29. (amended) [A] The method according to claim 24 wherein said [biased randomized candidate nucleic acids are biased to interact with a class of molecules selected from the group consisting of SH3 domains, SH2 domains, death domains, enzyme inhibitors, enzyme substrates and protease cleavage sites] randomized portion biased to interact with a class of molecules comprises the sequence set forth in SEQ ID NO:47, XXXPPXPXX, wherein X is a randomized residue.

30. (amended) [A] The method according to claim 23 or 24 wherein said [nucleic acids further comprise a] candidate bioactive peptide is fused to a nucleic acid sequence encoding a presentation sequence capable of presenting said [expression product] candidate bioactive peptide in a conformationally restricted form.

34. (amended) [A] The method according to claim 23 or 24 wherein said library comprises at least 10^5 [different nucleic acids] different retroviral nucleic acid sequences.

35. (amended) [A] The method according to claim 23 or 24 wherein said library comprises at least 10^6 [different nucleic acids] different retroviral nucleic acid sequences.

36. (amended) [A] The method according to claim 23 or 24 wherein said library comprises at least 10^7 [different nucleic acids] different retroviral nucleic acid sequences.

37. (amended) [A] The method according to claim 23 or 24 wherein said library comprises at least 10^8 [different nucleic acids] different retroviral nucleic acid sequences.

40. (amended) [A] The method according to claim [38] 23 or 24 wherein [said fusion partner is] candidate bioactive peptide is fused to a nucleic acid sequence encoding a rescue sequence.

41. (amended) [A] The method according to claim [38] 23 or 24 wherein [said fusion partner is] candidate bioactive peptide is fused to a nucleic acid sequence encoding a stability sequence.

42. (amended) [A] The method according to claim [38] 23 or 24 wherein [said fusion partner is] candidate bioactive peptide is fused to a nucleic acid sequence encoding a dimerization sequence.

43. (amended) [A] The method according to claim [38] 23 or 24 wherein [said fusion partner is] candidate bioactive peptide is fused to a nucleic acid sequence encoding a targeting sequence.

44. (amended) [A] The method according to claim 43 wherein said targeting sequence is selected from the group consisting of:

a) a localizing signal sequence capable of constitutively localizing said [translation product] candidate bioactive peptide to a predetermined subcellular locale;

b) a membrane-anchoring sequence capable of localizing said [translation product] candidate bioactive peptide to a cellular membrane; and

c) a secretory signal sequence capable of effecting the secretion of said [translation product] candidate bioactive peptide.

47. (amended) A molecular library of retroviruses comprising at least 10^5 different retroviral nucleic acid sequences [10^5 different biased randomized nucleic acids encoding a plurality of biased randomized peptides, wherein said biased randomized candidate nucleic acids are] wherein said retroviral nucleic acid sequences comprise an insertion of a nucleic acid sequence encoding a candidate bioactive peptide of from 4 to 100 amino acids in length, wherein said candidate bioactive peptide comprises a randomized portion biased to minimize stop codons.

48. (amended) [A] The molecular library of retroviruses according to claim 47 comprising at least 10^6 different [biased randomized nucleic acids encoding a plurality of biased randomized peptides] retroviral nucleic acid sequences.

49. (amended) [A] The molecular library of retroviruses according to claim 47 comprising at least 10^7 different [biased randomized nucleic acids encoding a plurality of biased randomized peptides] retroviral nucleic acid sequences.

50. (amended) [A] The molecular library of retroviruses according to claim 47 comprising at least 10^8 different [biased randomized nucleic acids encoding a plurality of biased randomized peptides] retroviral nucleic acid sequences..

51. (amended) A cellular library of mammalian cells containing a molecular library of retroviral constructs, said molecular library comprising at least 10^5 different [biased randomized nucleic acids encoding a plurality of biased randomized peptides, wherein said biased randomized candidate nucleic acids are biased to minimize stop codons] retroviral nucleic acid sequences, wherein said retroviral nucleic acid sequences comprise an insertion of a nucleic acid sequence encoding a candidate bioactive peptide of from 4 to 100 amino acids in length, wherein said candidate bioactive peptide comprises a randomized portion biased to minimize stop codons.

52. (amended) [A] The cellular library according to claim 51 wherein said constructs are integrated into the [cellular] genome of said mammalian cells.

54. (amended) [A] The molecular library of retroviruses according to claim [53] 47, wherein said [fusion partner comprises] candidate bioactive peptide is fused to a nucleic acid sequence encoding a targeting sequence.

55. (amended) [A] The molecular library of retroviruses according to claim [53] 47, wherein said [fusion partner comprises] candidate bioactive peptide is fused to a nucleic acid sequence encoding a rescue sequence.

56. (amended) [A] The molecular library of retroviruses according to claim [53] 47, wherein said [fusion partner comprises] candidate bioactive peptide is fused to a nucleic acid sequence encoding a stability sequence.

57. (amended) [A] The molecular library of retroviruses according to claim [53] 47, wherein said [fusion partner comprises] candidate bioactive peptide is fused to a nucleic acid sequence encoding a dimerization sequence.

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Retroviral cDNA Expression Libraries

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- Efficiently deliver highly complex libraries into mammalian cells
- Infects target cell line with nearly 100% efficiency
- Ideal for expression cloning applications

Retroviral cDNA Expression Libraries are high-complexity cDNA libraries in a retroviral expression vector. These libraries can be transferred into virtually any dividing cell type with nearly 100% efficiency to select for a desired phenotype using expression cloning. Additionally, the Tet-inducible libraries can be used for inducible expression of cDNA.

Retroviral Libraries are constructed in the pLIB vector, which allows the efficient transfer of inserts of up to 8 kb. Each Retroviral Library is provided both as purified plasmid sufficient for several packaging cell transfections and in *E. coli* for amplification. BD Biosciences Clontech offers several packaging cell lines. Retroviral Libraries are compatible with the ClonCapture™ cDNA Selection Kit. ClonCapture allows you to rapidly isolate target clones without traditional library screening

Tet-regulated control
With Tet regulation incorporated into the library, exceptionally tight control of cDNA expression can be achieved. Tet regulation also allows the induction of high-level expression for efficient screening. The Tet-Inducible Retroviral Library can be used with either the premade Tet-On™ or Tet- Off™ Cell Lines, or you can create your own stable Tet cell line using our plasmid or retroviral-based regulator vectors.

TOP

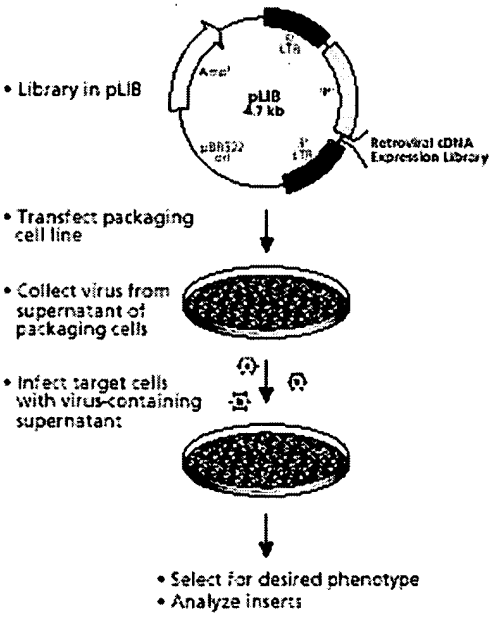

Figure 1. Retroviral library infection and expression

TOP

Product	Size	Cat.#
Human Brain Retroviral Library	pLIB	HL8006BB
Human HeLa Retroviral Library	pLIB	HL8002BB

Human Leukocyte Retroviral Library	pLIB	HL8007BB
Human Liver Retroviral Library	pLIB	HL8005BB
Human Mammary Gland Retroviral Library	pLIB	HL8001BB
Human Placenta Retroviral Library	pLIB	HL8000BB
Human Prostate Retroviral Library	pLIB	HL8003BB
Human Skeletal Muscle Retroviral Library	pLIB	HL8004BB
Mouse Embryo Retroviral Library	pLIB	ML8000BB
Rat Brain Retroviral Library	pLIB	RL8000BB

TOP

Components

RETROVIRAL cDNA LIBRARY
Library DNA
Library Culture (in *E. coli* DH10B)
pLAPSN
pLIB Control Vector
5' & 3' LIB Primers
User Manual (PT3230-1)
Vector Information Packet (PT3189-5)

TET-INDUCIBLE RETROVIRAL LIBRARY COMPONENT
Library DNA
Library Culture (in *E. coli* DH10B)
pRevTRE2 Vector
pRevTRE-Luc Control Vector
5' & 3' LNCX PCR/Sequencing Primers
User Manual (PT3352-1)
Vector Information Packet (PT3315-5)

TOP

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